JERUSSI CONSULTING, INC.

3311 Midland Road
Fairfax, Virginia 22031 USA

Tel: 703-273-3903 • Fax: 703-293-9161

'04 MAR -1 P1:32

February 19, 2004

Gary Buehler, Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration, HFD-600
7500 Standish Place
Rockville, MD 20855-2773

Docket No. 03P-0279/CPI

Dear Gary Buehler:

In response to your letter of February 3, 2004 please note the request for a full waiver regarding the Pediatric studies. The requisition is based on several impacting facts regarding the reference listed drug (RLD), Tri-Luma® Cream NDA 21-112. First, the indication and use for this product is the treatment of Melasma. This condition is not a pediatric disease. The conditions affects individuals primarily adult in age and more frequently found as a condition in pregnancy, suggesting the necessity of mature sexual steroid hormones.

Second, the product, Tri-Luma® Cream contains the corticosteroid fluocinolone acetonide. The topical use of corticosteroid derivatives in children has been noted with concern in numerous products. In particular, the package insert for Capex® Shampoo, Galderma, recites a **Precaution** in Pediatric use. Wherein the package insert states:

> "Safety and effectiveness in children and infants have not been established. Because of the higher ratio of skin surface to body mass, pediatric patients are at a greater risk than adults of HPA axis suppression when they are treated with topical corticosteroids. They are therefore also at greater risk of glucocorticoid insufficiency after withdrawal of treatment and of Cushing's syndrome while on treatment. Adverse effects including striae have been reported with inappropriate use of topical corticosteroids in infants and children.
>
> HPA axis suppression, Cushing's syndrome and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasma cortisol levels and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches and bilateral papilledema."

03P-0279 RC 2

Similar precautions are disclosed in other product package inserts of products containing fluocinolone acetonide, including the RLD, Tri-Luma® Cream. The package insert for the latter discloses as a **Precaution** that it contains the corticosteroid fluocinolone acetonide "Systemic absorption of topical corticosteroids can produce reversible hypothalamic-pituitary-adrenal axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment....."

Conclusion:

Based on the observations cited herein and on the absence of support by the Reference Listed Drug's manufacturer for Tri-Luma® Cream, I hereby request a full waiver under the "Pediatric Research Equity Act of 2003" (PREA) cited in your letter for the changes to the formulation requested in the suitability petition No. 03P-0279. Further, based on these observations, it would be unethical to request studies in this population because of the potential serious adverse effects that may be manifested by the Tri-Luma® Cream formula.

Sincerely,

Robert A. Jerussi

Robert A. Jerussi, Ph.D.